Science
qQH
431
.C357

Mendel's law and the heredity of albinism.

W.E. Castle and G.M. Allen

9 QH
431
C357

MENDEL'S LAW AND THE HEREDITY OF ALBINISM.

W. E. Castle and Glover M. Allen.

Reprinted from the Mark Anniversary Volume, Article XIX, pp. 379–398, 1903.

XIX.

MENDEL'S LAW AND THE HEREDITY OF ALBINISM.

W. E. Castle and Glover M. Allen.

SCIENCE
QH
431
C357

I. INTRODUCTION.*

Albinism, or the absence of the normal pigmentation of an organism, is a not infrequent phenomenon in both animals and plants, yet its occurrence in nature is sporadic and has usually been interpreted as an indication of organic weakness. But this interpretation is probably erroneous, for albino races of domesticated animals are apparently not inferior in vigor to other races. Such is demonstrably the case with albino mice.

The idea that albinos lack constitutional vigor may have its origin in the observation that, in crosses between albinos and normal individuals, no albino offspring are produced. But the disappearance of albinism in this case is not final. The albino character has not ceased to exist, but has merely become latent in the offspring. It will reappear unimpaired in the next generation if the cross-bred individuals be mated *inter se*.

The disappearance of the albino character for a generation, and its subsequent reappearance under close breeding, show that it is inherited in conformity with Mendel's law of heredity, and that it is, in the terminology of that law, a *recessive* character.

II. MENDEL'S PRINCIPLES OF HEREDITY.

The Mendelian principles of heredity, stated in the phraseology of present-day biology, are as follows:

1. Every gamete (egg or spermatozoön) bears the determinants of a complete set of somatic characters of the species. When two gametes meet in fertilization, there are accordingly present in the fertilized egg the representatives of two sets of somatic characters, which may or may not be the same. If they are the same for a given character, as, for example, coat-color in mammals, the individual which develops from the egg must inevitably have that same character. Thus, when gametes

* This paper contains a preliminary statement of certain results of breeding experiments with mice, guinea-pigs, and rabbits, which have been conducted in the Zoölogical Laboratory of Harvard University during the last two and a half years. The experiments with mice are the work principally of the junior author; those with guinea-pigs and rabbits, of the senior author.

formed by one white mouse, meet in fertilization gametes formed by another white mouse, the offspring are invariably white. Similarly, when a wild gray mouse is bred to another wild gray mouse, the offspring are invariably gray. And when a pure-bred spotted black-white mouse is bred to a mouse like itself, the offspring are all spotted black-white.

2. But when the two gametes uniting bear each what represents a different somatic character, only one of these characters may be manifested by the individual (or zygote) formed. Thus, when wild gray mice are mated with white mice, only gray offspring are produced. The gray character is, in Mendel's terminology, *dominant;* the white character, *recessive*. Or, when wild gray rats are mated with black-white rats, only gray rats are produced. The wild gray character is, accordingly, dominant not only over white, but also over black-white.

3. Sometimes the zygote formed by the union of two unlike gametes (hetero-zygote, Bateson, : 02) develops the character of neither parent in its purity. It may have a character intermediate between those of its parents, or something entirely different from either. Thus, when black-white mice are mated with white mice, the offspring are gray like the wild house-mouse.

4. Whatever the somatic character of the zygote is, the germ-cells which it forms will be, like those which united to produce it, half like the maternal and half like the paternal gamete. Thus a gray mouse obtained by crossing a wild gray mouse with a white one forms in equal numbers gametes which bear the gray character and those which bear the white character. This is conclusively shown by two simple breeding tests: (1) When a cross-bred (or hybrid) gray mouse is bred to a white mouse half the offspring are hybrid grays, half are white. This is precisely the result we should expect if the cross-bred gray mouse forms, as we have supposed, in equal numbers, gametes which bear the gray and those which bear the white character. For the gray mouse will produce

gametes . . . . . G and W;
the white mouse forms gametes. . . . . W and W;

the possible combinations of these two sets are. . . . . $2GW+2WW$.

But, as we have already stated, when a zygote contains *both* the gray character and the white character, only the former will be visible. This may be indicated by placing the W within a parenthesis. Further, in the expression $2\,WW$, one of the identical letters may be dropped as superfluous. Our formula then reads $2\,G(W)+2W$, and signifies that two in every four of the offspring produced will be gray hybrids, and

the remaining two white. (2) When two cross-bred (or hybrid) gray mice are bred together, the offspring consist of gray mice and white mice in the ratio of three gray to one white. Moreover, breeding tests show that of the three gray mice thus obtained one is pure, that is, will form only gametes bearing the gray character, while two are hybrid, that is, will form gametes some of which bear the gray character, others the white character. This is precisely the result expected under our hypothesis that each hybrid individual forms gametes, G and W, in equal numbers. For the possible combinations of two sets of gametes, each G and W, are represented by their product, $GG+2GW+WW$, or, simplified as already explained, $G+2\ G(W)+W$.

The principle illustrated by these examples is, as pointed out by Bateson (:02), the most fundamental and far-reaching of the Mendelian ideas. It is known as the "law of segregation," or "splitting" (de Vries, :00) of the parental characters at gamete-formation, or as the "principle of gametic purity" (Bateson, :02). Dominance is purely a secondary matter; it may or may not occur along with segregation, though the latter can be more easily demonstrated in cases where it is associated with the former. The principle of gametic purity rests upon the assumption that gamete-formation is the reverse of fertilization. In fertilization gametes A and B unite to form a zygote AB; when this zygote in turn forms gametes, they will be again A and B. From a knowledge of the *somatic form* alone of pure A's and B's, one can make no trustworthy prediction as to the form of AB. (Here is the fundamental error of the "law of ancestral heredity" as stated by Galton ('97) and by Pearson (:03). AB may have invariably the somatic form of A or of B (cases of simple dominance, as of gray over white in mice); or it may have *sometimes* the form of A, sometimes that of B (cases of alternative dominance—see Tschermak, :00); or, finally, the somatic form of AB may be different from both that of A and that of B (cases like that of the gray hybrid formed by the cross of black-white with white mice). But, no matter what the somatic form of AB is, we may with confidence predict that its gametes will be essentially pure A's and B's, and in equal proportions. This is the Mendelian expectation in all cases of alternative inheritance. Whether it applies to other cases also, and, if so, to what extent, is not yet known.

III. COMPLETE ALBINISM A RECESSIVE CHARACTER.

1. **In Mice.**—The recessive nature of complete albinism in mice has been conclusively demonstrated by Cuénot (:02), who, on crossing wild gray house-mice with albinos, obtained always gray mice indistinguishable in appearance from the pigmented parent. Yet these gray hybrids, when bred *inter se*, produced both gray

and white offspring approximately in the Mendelian ratio, 3 : 1. The exact numbers recorded are 198 gray : 72 white, or 26.6 per cent. albinos. According to Mendelian principles the grays of this second filial generation should consist in part of *pure* grays, which would not transmit the albino character, and in part of *hybrid* grays like their parents,—the first filial generation,—which would transmit alike the pigmented and the albino characters. This Cuénot demonstrated to be actually so, for certain pairs formed by random selection of the grays gave only gray offspring (189 individuals); the remaining pairs produced albino as well as gray offspring, and in the expected ratio, 3 grays : 1 albino. The precise numbers recorded are 162 grays : 57 albinos, or 26 per cent. albinos.

Cuénot's observations are fully substantiated by our own experiments, the results of which may be summarized as follows: Wild gray mice were crossed with albino mice; the offspring, sixty-four in number, were all gray like the wild parent, though a single litter of three young, which died without attaining their full growth, were of a somewhat lighter gray than the wild parent. Certain of the cross-breds were paired together, and produced 66 offspring, 42 of which were gray, 24 white. This is a considerable deviation from the expected ratio, 3 : 1, but it should be remembered that the total number is relatively small. The result is of the *nature* expected, in that both gray and albino offspring are produced, and of the former a larger number than of the latter.

To determine whether the grays are, as expected, of two sorts, one hybrid, the other pure, six pigmented individuals have been crossed with the parental white stock. Three of the six have thus far produced only pigmented offspring, indicating that they are pure; the other three have produced both gray offspring and white offspring, showing that they are hybrids. The two sorts of offspring produced in the case last mentioned should, according to Mendelian expectation, be equally numerous. The numbers thus far recorded are 35 pigmented individuals: 23 albinos, a result agreeing with expectation in that both gray and white offspring are produced, though these are not in the exact proportions demanded by Mendel's laws.

If we *combine* the results of this cross with those obtained by interbreeding hybrids of the first filial generation, we get for the whole a close agreement between expectation and observation. The expectation is 78.5 gray : 45.5 white; the observed result is 77 gray : 47 white.

White mice obtained by one or the other of these crosses have repeatedly been bred together, but without the occurrence of a single exception to the expected Mendelian result, the offspring being invariably albinos.

A further test of the Mendelian hypothesis as applied to albinism in mice was

made by Cuénot. By back-crossing hybrid grays with the ancestral white stock he obtained gray as well as white individuals, which in the phraseology of breeders should be $\frac{1}{2}$, $\frac{3}{4}$, $\frac{7}{8}$, etc., white "blood," yet all the grays, irrespective of ancestry, gave precisely similar results in crosses with whites, viz., equal numbers of gray and white offspring.

It is evident, then, that when a pure gray race of mice is crossed with a pure white race, the gray character invariably dominates in the offspring, and in subsequent generations both gray individuals and white individuals occur approximately n the proportions demanded by Mendel's principles of dominance and segregation. No better illustration of Mendel's law has yet been produced than is afforded by the cross between gray and white mice.

2. In Other Mammals, in Fishes, and in Plants.—In the case of guinea-pigs, we have many times mated together albinos born of mottled parents, or obtained by mating a mottled with a white animal, but never with any but the expected Mendelian result, all the young being albinos.

In the case of rabbits, the same law appears to hold. Professor R. T. Jackson kindly placed at our disposal last summer three white rabbits, a male and two females, all born in the same litter, of spotted parentage. The two females have borne by their brother, in three litters, seventeen young, all albinos.

In man, Farrabee (:03) and Castle (:03) have recently shown albinism to be in all probability recessive.

As to fishes, Dr. Hugh M. Smith, of the United States Fish Commission, informs us that in one of the State fish-hatcheries of this country there is bred as a curiosity a race of albino trout which "*breed true*," indicating that the albino character is recessive.

In plants more than two-thirds of the Mendelian cases mentioned by de Vries (:02, p. 146) are cases of "depigmentation" of flowers or fruit, the depigmented condition being invariably recessive in crosses with the normal condition.

It appears, then, that in organisms in general albinism behaves as a recessive character in heredity.*

* The only exception known to the writers is the dominance of white plumage, in certain crosses of poultry, as recorded by Bateson and Saunders (:02). Yet the dominant character in this case is one of *partial* albinism only, and its dominance is not invariable. We suspect that the dominance of white plumage results from its *coupling* in the gametes with some other character strongly dominant by nature.

IV. PARTIAL ALBINISM A MOSAIC OF DOMINANT AND RECESSIVE CHARACTERS, AND A UNIT IN HEREDITY.

Darbishire (:02, :03) finds that in crosses between a peculiar race of partial albino mice and true albinos, the albinism does not entirely disappear in the offspring, and he thinks that this weighs heavily against the entire Mendelian hypothesis. In reality Darbishire's observations, when rightly interpreted, afford strong evidence in favor of that hypothesis. It may be well, therefore, to examine them with some care. But before doing so one or two earlier observations should be noticed.

Haacke ('95) crossed spotted blue-[black-]and-white Japanese dancing mice with albino mice, and obtained offspring uniformly gray in color, like the wild house-mouse, or uniformly black. Occasionally, however, one of the gray or black offspring bore a fleck of white on forehead or belly.

Von Guaita ('98, :00) repeated the experiment, crossing spotted black-and-white Japanese dancing mice with an inbred stock of albinos. He obtained twenty-eight young, all uniformly gray like the house-mouse. These gray mice bred *inter se* yielded in subsequent generations gray, gray-white, black, black-white, and white offspring.

Darbishire's experiment consisted in crossing albino mice with a peculiar race of Japanese dancing mice which had *pink eyes* and were uniformly white except for patches of pale fawn-color on the cheeks, shoulders, and rump. The dancing mice had been tested and found to breed true *inter se*. From the cross between these partial albinos and true albinos a total of 203 young was obtained, all dark-eyed and with bodies more or less extensively pigmented. As to color, which is recorded for all except the latest litters, the hybrids show the following distribution: 7 yellow: 138 gray : 9 black. Of these, seventy-eight gray and six black mice were spotted more or less extensively with white, while the seventy unicolored mice were, all except one, of a lighter color on the belly and tail. In only three out of the entire one hundred and fifty-four for which a full record of the coloration is given, is the pigmentation less extensive than in the pigmented parent. Even in these three the intensity of the pigmentation had been increased by the cross, for the offspring were *gray* pigmented, whereas the pigmented parent had been merely spotted with light fawn.

Darbishire's experiment is instructive in a number of ways:

1. It completely confirms the conclusion based upon the experiments of Crampe ('85), Haacke ('95), von Guaita ('98, :00), Cuénot (:02), and ourselves (Castle and

Allen, :03) that, in crosses between pure races of pigmented and albino mice, the pigmented character invariably dominates in the offspring.

2. It shows that cross-breeding may bring into activity latent characters or latent elements of a complex dominant character. The pigmented parent in Darbishire's crosses bore only yellowish ("fawn") pigment, but the hybrid offspring produced by a cross with albinos, in all except sixteen out of one hundred and fifty-four cases, bore also black pigment, which when present with yellow produces the complex character *gray*. In nine of the sixteen cases mentioned black pigment alone was present, and in the remaining seven cases yellow pigment alone was present.

3. These facts show that cross-breeding may cause one element of a dominant character to disappear (become latent), while a different element (previously latent) takes its place. This is what happened in nine of the sixteen cases mentioned; in these nine cases fawn (present in the pigmented parent) disappeared, while black (undoubtedly latent in one or both parents) became active.

Darbishire is unable to regard albinism as beyond qualification recessive, in the Mendelian sense, because white does not entirely disappear from the bodies of the offspring in his first cross. The condition observed by him is indeed somewhat unusual, though entirely in harmony with Mendelian principles. The thing which demands explanation in such cases as this is, not that the *offspring* are spotted, for this may be regarded as a case of simple dominance of the character of the pigmented parent, but the fact that the dominant and recessive characters occur together *in the spotted parent*. Two explanations have been offered for such (mosaic) conditions. Correns (:03) regards mosaic individuals as due to alternative dominance of the two parental characters. He considers the anlagen of both characters to be present together throughout the soma, but in one region of the body one character dominates, in another region the other. He supports this idea with the observation that in particolored flowers which bear stamens, some in the pigmented, others in the unpigmented parts of the flower, pollen taken from stamens of either region transmits both the pigmented (dominant) and the unpigmented (recessive) characters. This observation, however, proves only that the *germ-cells* may have a character different from that of the soma. The assumption made by Correns that soma and germ-cells are of the same nature in particular regions of the flower is, in our opinion, without sufficient warrant.

The facts observed by Darbishire, as well as certain observations of our own, accord better with a different explanation, suggested by Bateson and Saunders (:02). On this view, which one of us has recently elaborated (Castle, :03[a]), a mosaic condition of the soma is due to a mosaic condition of the germ which produced the mosaic

individual. Strong evidence in support of this view is afforded by the experiments of Haacke, von Guaita, and Darbishire, as well as by our own experiments, in crossing spotted with albino mice. We bred to albino females two spotted males of a black-white stock whose individuals bred true *inter se*. The offspring were like those obtained by Haacke in crossing Japanese dancing mice with albinos, namely, mice uniformly gray or black in color, though sometimes with a fleck of white on the belly, or with one or more white bands on the tail. Of the forty-three young produced by this cross, twenty-eight were gray and fifteen black. The fact that no albino offspring were produced shows that the spotted males formed no recessive gametes, but only those which were either mosaic or else purely dominant in character. But if dominant gametes had been formed by segregation from a dominant-recessive mosaic, we should expect that by a residual process *recessive* gametes would be formed also. The latter not having been formed, it is safe to suppose that the former were not formed either, but that *all* the gametes formed by these spotted males were *mosaic*.

That the albino character entered as a latent constituent into the gray or black hybrids formed by the cross just described is shown conclusively by the character of their offspring. When bred *inter se* they produced albino as well as pigmented offspring, and approximately in the ratio, 1 : 3; or, when bred to albinos, in the ratio 1 : 1.

Accordingly, in the original cross described, we have a case of simple dominance of the pigment-forming over the albino character. This dominance is attended, in about two cases out of three, by reversion to the particular form of pigmentation found in the wild house-mouse. The reversion is due to the coming into activity of a capacity (previously latent) to form *yellow* pigment, which with black pigment forms gray. This latent capacity must have been present in one or the other or possibly in *both* of the parents crossed.

Darbishire's results differ from ours only in degree, not in kind. He, too, gets invariably dominance of the pigment-forming over the albino character, and this is associated in all except sixteen out of one hundred and fifty-four cases with reversion to the ancestral *kind* of pigmentation, gray. The chief differences between his results and our own are as follows:

1. In our experiments *yellow* was the latent constituent of gray which was brought into activity by a cross with albinos; in the experiments of Darbishire *black* was the latent constituent brought into activity.

2. In our experiments white disappeared for the most part from the bodies of the hybrids; but in Darbishire's experiments the disappearance of white was much less complete. There was a strong tendency for the mosaic gamete to *dominate as*

a unit without serious disturbance of the balanced relationship of pigmented and unpigmented areas in the mosaic structure. This tendency is observable in eighty-four of the one hundred and fifty-four cases recorded. Of the remaining seventy cases, sixty-seven are quite comparable with our own. In sixty of them the black character, latent in one or possibly in both parents, has become active and combining with yellow (fawn) visible in the pigmented parent, has formed gray. In seven cases black, if present, has remained latent, and the offspring are simply yellow-pigmented. But in the case of three black and of six black-white hybrids, this curious result is observed: the pigmented character (yellow) visible in the dark parent disappears entirely, while black takes its place.

In Darbishire's experiments, as in our own, the effect of a cross with albinos is to release the dominant character from the strict localization which it had in the mosaic parent. In Darbishire's mosaic mice the localization of pigment was much more rigid than in our own. His mice bore pigment only on the shoulders and rump and had *pink* eyes; ours were pigmented over at least half of the body and had *black* eyes. It is not surprising, then, that the pigmentation should be less extensive in Darbishire's hybrid mice than in our own. Yet it is evident that in all his hybrids there occurred release, more or less complete, of the pigment-forming character from its localization in the original mosaic. In every case the hybrid had pigmented eyes, though neither parent possessed this character.

V. PURE AND HYBRID MOSAICS.

In our experiments in crossing spotted with albino mice, a third black-white male was employed. He was a half-brother to the two spotted males previously mentioned, born of the same mother but by a different sire. The white areas on his body were less extensive than those on his two brothers. He was bred to the same stock of white females as they, but with different results. By him the albinos bore albino as well as pigmented offspring; of the former twenty-one, of the latter twelve, ten being gray and two black. The albino offspring were found in this case, as in all others tested, to breed true *inter se*.

It is evident that the third black-white male differed in nature from his two half-brothers, for he formed *recessive* gametes, whereas they did not.

Examination of other breeding records of spotted mice kept by us during the past two years shows that it is possible in these also to distinguish two different sorts of mosaic individuals. These are:

1. *Pure mosaics,* spotted and forming only mosaic gametes, *DR.* They breed true *inter se,* but when crossed with albinos produce only individuals of the following class.

2. *Hybrid mosaics,* usually *more extensively pigmented than pure mosaics,* often pigmented all over. (Compare the results of Haacke, von Guaita, and Darbishire.) They form, in approximately equal numbers, mosaic and recessive gametes, *DR* and *R,* respectively. Accordingly, when bred *inter se,* they produce offspring of three different sorts, *DR, DR·(R)* [or *D(R)·(R)*],* and *R,* that is, pure mosaics, hybrid mosaics, and recessives. Theoretically these three classes of offspring should be numerically as 1 : 2 : 1. There is reason to believe that these proportions are approximated in our experiments, but this matter has not yet been fully tested. When bred to albinos, hybrid mosaics produce (in equal numbers) hybrid mosaic and albino offspring.

It is possible to recognize in the experiments of von Guaita and Darbishire also these two different classes of mosaics. Von Guaita's original stock of dancing mice consisted of *pure* mosaics, for they bred true *inter se,* and when bred to albinos produced only pigmented offspring. These offspring, though not themselves spotted, were clearly *hybrid mosaics,* for when bred *inter se* they produced spotted as well as albino offspring, of the former nine, of the latter fourteen, in a total of forty-four young; the expectation on our hypothesis is eleven of each!

The evidence afforded by Darbishire's mice is even more convincing because of a visible difference between the heterozygous (hybrid mosaic) form and both of the pure parental forms. The parents were, as we have seen, in every case pink-eyed, whereas the hybrids were as invariably dark-eyed. Hybrids bred *inter se* should in this case, according to our hypothesis, produce pure mosaics (pink-eyed), hybrid mosaics (dark-eyed), and albinos, in the proportions, 1 : 2 : 1. These three sorts of individuals were actually observed by Darbishire, and in very nearly the theoretical proportions. In a total of sixty-six young the observed numbers are 17 pink-eyed mosaics : 36 dark-eyed individuals : 13 albinos; the expectation is 16.5 : 33 : 16.5. By crossing hybrids with albinos Darbishire obtained, as we should expect on the hypothesis stated, only two of the three classes produced by intercrossing hybrids, namely, dark-eyed individuals (hybrid mosaics) and albinos; no *pink-eyed* pigmented individuals were produced. The expectation is that the two classes formed will in this case be approximately equal; the observed numbers are 94 dark-eyed individuals, 111 albinos.

* The period is used to indicate the distinctness, in the zygote, of the gametes which united to form that zygote, as well as to show that, when in the hybrid individual segregation of characters takes place at gamete-formation splitting will occur at the point marked by the period, producing gametes *DR* and *R.*

The idea that there are, as just explained, two different sorts of mosaic individuals originated with the junior author of this paper. It constitutes a discovery of no small importance, one which lends strong support to the Mendelian hypothesis of essential gametic purity. It shows that alternative parental characters, when united in fertilization, do not mix, but that each retains its own identity and subsequently separates from the other when gametes are formed. This takes place *even when one of the parental characters is itself a mosaic!* Herein we have a confirmation of the conclusion based upon morphological observations, that the paternal and maternal contributions to the zygote retain each a distinct individuality. Further, the idea of Bateson receives confirmation, that the gray color of mice obtained by crossing black-white with white mice is itself a "heterozygote" character.

VI. PURE AND IMPURE RECESSIVES.

Although certain of Darbishire's conclusions are, as we have seen, untenable, he has made observations of great significance, one of which deserves particular notice. In his crosses with dancing mice he employed two different stocks of white mice, and with results somewhat different in the two cases. The two stocks were (1) "pure-bred" albinos purchased from breeders, and presumably descended from white parents, and (2) "cross-bred" albinos known to be descended from spotted (i.e., hybrid mosaic) parents. The latter when crossed with the fawn-white dancing mice produced twenty-five offspring spotted with white, and only four which were pigmented all over. The "pure-bred" albinos when similarly mated produced thirty-six spotted mice and sixty-one mice pigmented all over. In other words, the cross with "pure-bred" albinos produced a much smaller proportion of spotted mice than did that with "cross-bred" albinos.

Apparently the primary effect of a cross between a mosaic and an albino individual is to release in the soma of the offspring the dominant character either latent or tied up in a firm mosaic with the recessive character in the gametes of the spotted parent. The dominant character is thus free to extend its influence over the entire soma of the hybrid offspring. This release seems to be the more complete the more free the albino stock has been kept from crosses with pigmented animals.

It follows from Darbishire's observation that *not all albinos breed alike* when crossed with the same pigmented stock, a conclusion which our own experiments fully substantiate. This indicates that *the gametes formed by different albino stocks are not*

all alike, and raises the question whether all are equally *pure* as regards the pigment-forming character.

Construed in the strictest sense, the doctrine of gametic purity is untenable. We cannot accept that interpretation of it which requires that the gametes formed by an individual be the *precise equivalents,* in all particulars, of the respective gametes which united to form that individual. Mendel himself would not have assented to such an interpretation, for in the latter part of his original paper ('66) he clearly states the important principle that a composite character may undergo resolution into its elements in consequence of crossing. This allows a *part* of a complex character to pass into one gamete, while the remaining parts pass into another; in other words, it makes possible the formation of *mosaic gametes,* into whose composition the dominant and recessive characters may *both* enter in varying degree. All gametes which contain *any portion* of a dominant or of a recessive character associated with its opposite, are in reality *mosaic;* yet if a gamete essentially recessive contains only *traces* of the dominant character, it may be convenient to recognize this fact in its designation, which we do by calling it an *impure* recessive.

In guinea-pigs the impurity of recessives tainted with the dominant character is commonly visible. Ordinary white guinea-pigs with pink eyes, though they invariably produce albinos when bred *inter se,* have a greater or less amount of sooty black pigment in the skin and hair of their ears, nose, and feet, showing the presence of a trace of the dominant character. Rarely is it possible to obtain an animal free from this visible taint, and even when obtained, we are informed by breeders, such individuals are likely to produce offspring with a certain amount of pigment on their ears or feet.

The so-called Himalayan rabbit is another illustration of a mosaic with a predominantly recessive (albino) character, in which the dominant (pigment-forming) character is localized precisely as in the impure albino guinea-pig, namely, at the extremities. Himalayan rabbits have brownish-black noses, ears, feet, and tails, being elsewhere snowy white and having pink eyes. They breed true *inter se,* yet, according to Darwin ('76, p. 114), may occasionally produce a silver-gray animal, in which the pigment is not restricted to the extremities. This condition must result from *liberation* of the dominant character from the strict localization which it has in ordinary individuals and which it must have also in the gametes that produce them.

In mice, on the other hand, impurity in recessive individuals is not visible, though doubtless sometimes present. So long as the breeder wishes only to obtain white mice, it makes no difference what the ancestry of his breeding animals is. All albinos alike will produce only white offspring when bred to albinos. But if the breeder

desires to cross his albinos with colored mice, the pedigree of the former is of consequence. Different albinos will, in crosses with the same pigmented stock, yield different results. This is shown both by Darbishire's experiments and by our own. In October, 1900, we began a breeding experiment in which a family of black-white mice was crossed with two different stocks of albino mice. All three stocks bred true among themselves; but in crosses with the black-whites one albino stock produced only gray or black offspring, whereas the other produced *no gray* offspring, but only black or fawn-colored ones, often extensively spotted with white. Manifestly the gametes formed by the two albino stocks, though all predominantly recessive, were not all alike. It is probable that some of them at least were impure, containing traces of a latent pigment-forming character. Such a latent character is apparently not liberated, in the case of mice, by a cross with a different stock of albinos; but this result can be secured, probably, by a cross with dominants. We infer this not only from the observed result in crosses between black-white and albino mice, but also from what has been observed to take place in guinea-pigs. On crossing a "dark-pointed" albino guinea-pig with a stock of red guinea-pigs which for a number of generations had bred true *inter se*, there were obtained offspring which in every instance were predominantly *black* in color, yet with a certain proportion of red hairs mixed with the black, which gave them a "brindle" or finely mottled black-and-red appearance. This result must be attributed to a liberation of the black-pigment-forming character either from its visible, strict localization in the albino parent, or from a possible latent and invisible occurrence in the red parent. We incline at present toward the former explanation, but the matter has not yet been fully tested. The complete disappearance of the albino character in this cross is noteworthy as being parallel to its behavior in the cross between black-white and white mice.

Darbishire's pink-eyed, fawn-white dancing mice were mosaics predominantly recessive, and might with some propriety be designated *impure* recessives, but they differed from impure guinea-pig recessives and from Himalayan rabbits in that, when crossed with ordinary recessives, they did not produce pink-eyed animals like themselves, but rather animals which were in a majority of cases extensively pigmented. It seems more appropriate, therefore, to designate them *mosaics*.

"Dutch-marked" varieties of guinea-pigs, rabbits, and mice, and the somewhat similarly marked Holstein and Hereford cattle, though they do not breed so true *inter se* as dark-pointed albino guinea-pigs or Himalayan rabbits or, perhaps, as pink-eyed dancing mice, nevertheless indicate a fairly precise localization of the pigment-forming and albino characters within mosaic germs.

If we adopt the Roux-Weismannian idea of the nature of the chromosomes, it

is probable that particular chromosomes, or part chromosomes, in the mosaic germ, contain the dominant character, while the remaining chromosomes, or part chromosomes, contain the recessive character.

VII. CROSS-BREEDING, REVERSION, AND THE DOCTRINE OF GAMETIC PURITY.

Union with a recessive gamete usually, though not always, serves to break up this localization, allowing the dominant character to extend its influence throughout the entire body. This is the case, for example, in the cross between spotted and white mice in the experiments of Haacke, von Guaita, and in part of Darbishire, as well as in our own. It is possible to suppose in such cases either (1) that the resolving effect of the cross is restricted to the soma of the cross-bred, or (2) that it extends also to the germ-cells of the cross-bred. If the former hypothesis is correct, the cross-bred should form gametes *DR* and *R* in equal numbers; if the latter, then only gametes *D* and *R* should be formed, and these in equal numbers. A simple test is afforded by the breeding *inter se* of hybrid mice produced by crossing pure mosaics with recessives. On the first hypothesis suggested, the offspring of the hybrids should consist, in at least one case out of four, of *spotted* mice formed by the union of two pure *DR* gametes; on the second hypothesis *no spotted* mice should be produced, but only classes *D*, *D*(*R*), and *R*, as in breeding together hybrids between wild gray mice and white mice. Von Guaita's experiments show the formation at the second filial generation of *nine spotted mice*, twenty-one uniformly gray or black mice, and fourteen white mice. The expectation on hypothesis (1) is 11 spotted : 22 gray or black : 11 white mice, which approximates closely the observed result; whereas on hypothesis (2) there should be *no* spotted mice, but only such as are pigmented all over or else are albinos. The result is conclusive in favor of hypothesis (1)—that a mosaic gamete, on uniting in fertilization with a recessive gamete, does not lose its own identity nor undergo resolution into its constituent parts.*

Yet we must not fail to observe that a cross of the sort just described is not without its effects on the nature of the gametes; these do not retain their original character. For whereas the mosaic gametes of the original spotted parents produced, on union in pairs, invariably black-white offspring, the mosaic gametes formed by their hybrid offspring, when similarly combined, formed in von Guaita's experiments eight *gray*-white offspring, but only one *black*-white. Accordingly, though it seems certain that mosaic gametes may in crosses retain their mosaic character, the cross is nevertheless

* Compare the results of Darbishire, as stated on p. 390.

able to bring into activity characters latent in the parents, and to add these to the previous visible total of the mosaic, giving it thus a new character. In the original black-white stock the mosaic consisted of the active characters, black and white, while the character yellow was latent either in the mosaic gametes or in the recessive gametes with which they united when the cross was made. The cross brought at once into activity the latent character, yellow; and this combined with black to form the composite dominant character, *gray*, while white, though present in *both* gametes uniting, usually became for the time being altogether latent. But the gametes formed by the gray hybrid were not, as we should expect on the principle of strict gametic purity, *black*-white and white, but *gray*-white and white respectively. The character yellow, latent previous to the cross, having once become active remained so.

In Darbishire's experiments the cross with albinos served in most cases to bring latent black into activity along with yellow (seen in the pigmented parent), but in a few cases yellow (previously active) disappeared in the offspring, while black (previously latent) replaced it.

By these experiments we are put in possession of a principle of great importance, both theoretical and practical. It modifies essentially the Mendelian doctrine of gametic purity as commonly understood, yet without denying the soundness of that doctrine at core. It allows the breeder (as breeders habitually do) to reap substantial benefit from crosses, for, in addition to permitting him to secure new combinations of the elementary characters visible in the parents crossed, it places at his disposal characters latent in the parents, and particularly facilitates the reacquisition of lost characters.

The gray of hybrid mice obtained as in von Guaita's experiments is a composite character resulting from the combination of visible black with latent yellow. In Darbishire's experiments it results from the combination of visible yellow with latent black. In either case gray is obtained by synthesis (Bateson) of black and yellow. This view is supported by the observation of the reverse of this process, in crossing wild gray with white mice. In the second and later hybrid generations *black* pigmented as well as gray pigmented mice are obtained. These must result from a resolution of gray into its constituent elements, black and yellow, of which the latter then becomes latent.

It is not necessary to suppose, as Mendel apparently did, that the segregated elements of a composite character pass invariably into different gametes. There is reason to believe that yellow is frequently, if not always, latent in black mice, and black in yellow mice, though such an occurrence has not yet been conclusively demonstrated.

We would not, however, deny the possible correctness of Mendel's explanation in other cases. This should be indicated in breeding experiments by the simultaneous appearance in different individuals of the segregated elements of the composite character, and in particular numerical proportions. Each new sort should be incapable of producing the other, under either close or cross breeding. This is a subject well meriting more careful investigation.

VIII. SUMMARY.

1. Complete albinism, without a recorded exception, behaves as a recessive character in heredity.

2. Partial albinism is a mosaic condition in which the dominant pigment-forming character and the recessive albino character are visible in different parts of the same individual.

3. Pure mosaic individuals form only gametes which partake of their own mosaic nature. They and their gametes may be designated *DR*.

4. Hybrid mosaics result from the union of a mosaic gamete, *DR*, with a recessive gamete, *R*, as in a cross between a pure mosaic and a recessive individual. Such crosses are made when a race of spotted mice which breeds true is crossed with albinos.

5. Hybrid mosaic mice are usually more extensively pigmented than pure mosaics, frequently they are pigmented all over. When they are spotted with white, we may consider this the result of dominance of the mosaic gamete *as a unit* and may designate them accordingly, $DR \cdot (R)$. When they are pigmented all over, it is clear that the *dominant element* only of the mosaic gamete is visible in them. They should then be designated $D(R) \cdot (R)$.

6. The gametes formed by a hybrid mosaic are of two sorts, like those which united to produce it, namely, *DR* and *R*. Accordingly when hybrid mosaic individuals breed together they produce offspring of three different sorts—pure mosaics, hybrid mosaics, and recessives. We should expect these three classes to be numerically as 1 : 2 : 1, and this is probably the case. When a hybrid mosaic is bred to a recessive, two sorts of offspring are produced—hybrid mosaics and recessives. These classes should be of approximately equal size.

7. Albinism apparently complete may in reality conceal traces of the pigment-forming character either in an active or in a latent condition. Albinos that are thus constituted are in reality mosaics of the contrasted characters, but with the pigment-forming character (ordinarily dominant) occurring in a condition of partial or com-

plete latency. When bred to other albinos they uniformly produce albinos, hence they may for convenience be distinguished as *impure* recessives. In guinea-pigs and rabbits the impurity of recessive individuals is, in certain cases at least, visible; in mice it apparently is not.

8. Cross-breeding is able to bring into activity latent characters or *latent elements* of a complex character. This is probably the true explanation of many cases of reversion. Conversely, it is able to cause one or another element of a complex character to *become latent* and to *remain* so under close breeding. This principle probably explains how races of black or yellow mice may be obtained by crossing wild gray mice with albinos.

9. The Mendelian doctrine of gametic purity is fully substantiated by experiments in breeding mice, guinea-pigs, and rabbits, but with the important qualification stated under 8, a qualification which really enhances the practical utility of that doctrine in its every-day application by breeders.

IX. BIBLIOGRAPHY.

Bateson, W.
:02. Mendel's Principles of Heredity: a Defence. With a Translation of Mendel's Original Papers on Hybridisation. Cambridge, Eng., 16°, xiv+212 pp.

Bateson, W., and Saunders, E. R.
:02. Experimental Studies on the Physiology of Heredity. Reports to the Evolution Committee of the Royal Society. Report I. 160 pp. London.

Castle, W. E.
:03. Note on Mr. Farabee's Observations [on Negro Albinism]. Science, n. ser., vol. 17, no. 419, pp. 75–76.

Castle, W. E.
:03[a]. Mendel's Law of Heredity. Proc. Amer. Acad. Arts and Sci., vol. 38, no. 18, pp. 535–548.

Castle, W. E., and Allen, G. M.
:03. The Heredity of Albinism. Proc. Amer. Acad. Arts and Sci., vol. 38, no. 21, pp. 603–622.

Correns, C.
:03. Ueber Bastardirungsversuche mit Mirabilis-Sippen. Erste Mittheilung. Ber. Deutsch. Bot. Gesell.; Bd. 20, Heft 10, pp. 594–608.

Crampe, [H.]
'85. Die Gesetze der Vererbung der Farbe. Landwirtsch. Jahrbücher, Bd. 14, Heft 4, pp. 539–619.

Cuénot, L.
:02. La loi de Mendel et l'hérédité de la pigmentation chez les souris. C. R. Acad. Sci., Paris; tom. 134, pp.; 779–781.

Darbishire, A. D.
:02. Notes on the Results of Crossing Japanese Waltzing Mice with European Albino Races. Biometrika vol. 2, pt. 1, pp. 101–104.

Darbishire, A. D.
:03. Second Report on the Results of Crossing Japanese Waltzing Mice with European Albino Races. Biometrika, vol. 2, pt. 2, pp. 165–173.

Darwin, C.
'76. The Variation of Animals and Plants under Domestication. Second Edition, revised. New York, 8°, 2 vols., xiv+473, x+495 pp.

Farabee, W. C.
:03. Notes on Negro Albinism. Science, n. ser., vol. 17, no. 419, p. 75.

Galton, F.
'97. The average Contribution of each several Ancestor to the total Heritage of the Offspring. Proc. Roy. Soc. London, vol. 61, pp. 401–413.

Guaita, G. v.
'98. Versuche mit Kreuzungen von verschiedenen Rassen der Hausmaus. Ber. naturf. Gesellsch. zu Freiburg, Bd. 10, pp. 317–332.

Guiata, G. v.
:00. Zweite Mittheilung über Versuche mit Kreuzungen von verschiedenen Rassen der Hausmaus. Ber. naturf. Gesellsch. zu Freiburg, Bd. 11, pp. 131–138, 3 Taf.

Haacke, W.
'95. Ueber Wesen, Ursachen und Vererbung von Albinismus und Scheckung und über deren Bedeutung für vererbungstheoretische und entwicklungsmechanische Fragen. Biol. Centralbl., Bd. 15, pp. 44–78.

Mendel, G.
'66. Versuche über Pflanzenhybriden. Verh. naturf. Vereins in Brünn, Bd. 4, Abt., pp. 3–47. [Translation in Bateson, :02.]

Pearson, Karl.
:03. The Law of Ancestral Heredity. Biometrika, vol. 2, pt. 2, pp. 211–236.

Tschermak, E.
:00. Ueber künstliche Kreuzung bei Pisum sativum. Zeitsch. f. landwirths. Versuchswesen in Oesterreich, Jahrg. 3, pp. 465–555.

Vries, H. de.
:00. Sur la loi de disjonction des hybrides. C. R. Acad. Sci., Paris, tom. 130, pp. 845–847.

Vries, H. de.
:02. Die Mutationstheorie. Leipzig, 8°, Bd. 2, Die Bastardirung, Lief. 1; 240 pp., 2 Taf.

DATE DUE

DEC 1 1978

DEC 15 1978

GAYLORD PRINTED IN U.S.A.

qQH431 C357 SCIII
3 5002 00048 3151
Castle, William E.
Mendel's law and the heredity of albinis

Science qQH 431 .C357

Castle, William E.
1867-1962.

Mendel's law and the
heredity of albinism